WEST Search History

DATE: Tuesday, April 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L6	L1 and erectile	10	L6
L5	L3 and erectile	2	L5
L4	L3 and topical$	29	L4
L3	L1 and (nitric adj1 oxide)	37	L3
L2	L1 and (NO or nitric adj1 oxide)	1718	L2
L1	ascorb$ adj2 palmitate	1853	L1

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 29 of 29 returned.

☐ 1. Document ID: US 6555700 B1

L4: Entry 1 of 29 File: USPT Apr 29, 2003

US-PAT-NO: 6555700
DOCUMENT-IDENTIFIER: US 6555700 B1

TITLE: 1,3-propane diol esters and ethers and methods for their use in drug delivery

DATE-ISSUED: April 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Horrobin; David Frederick	Guildford			GB
Manku; Mehar	Carlisle			GB
McMordie; Austin	Carlisle			GB
Knowles; Philip	Carlisle			GB
Redden; Peter	Nova Scotia			CA
Pitt; Andrea	Carlisle			GB
Bradley; Paul	Carlisle			GB
Wakefield; Paul	Carlisle			GB

US-CL-CURRENT: 554/227

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6555573 B2

L4: Entry 2 of 29 File: USPT Apr 29, 2003

US-PAT-NO: 6555573
DOCUMENT-IDENTIFIER: US 6555573 B2

TITLE: Method and composition for the topical treatment of diabetic neuropathy

DATE-ISSUED: April 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rosenbloom; Richard Allen	Elkins Park	PA		

US-CL-CURRENT: 514/456; 514/458, 514/474, 514/725, 514/733

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6531608 B2

L4: Entry 3 of 29 File: USPT Mar 11, 2003

US-PAT-NO: 6531608
DOCUMENT-IDENTIFIER: US 6531608 B2

TITLE: Various thiol complexes, processes for their synthesis and clinical applications

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pearson; Don C.	Lakewood	WA		
Richardson; Kenneth T.	Anchorage	AK		

US-CL-CURRENT: 548/182; 556/110, 556/118, 556/45, 562/557

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 4. Document ID: US 6521271 B1

L4: Entry 4 of 29 File: USPT Feb 18, 2003

US-PAT-NO: 6521271
DOCUMENT-IDENTIFIER: US 6521271 B1

TITLE: Compositions and methods of treatment for skin conditions using extracts of turmeric

DATE-ISSUED: February 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Phan; Dung	San Jose	CA	95121	

US-CL-CURRENT: 424/756; 424/59, 424/60, 424/62, 514/165, 514/557, 514/729, 514/730, 514/731, 514/732

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 5. Document ID: US 6506765 B2

L4: Entry 5 of 29 File: USPT Jan 14, 2003

US-PAT-NO: 6506765
DOCUMENT-IDENTIFIER: US 6506765 B2

TITLE: Apomorphine derivatives and methods for their use

DATE-ISSUED: January 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gupta; Pramod K.	Gurnee	IL		
Milkowski; Deborah	Chicago	IL		
Sutkowski-Markmann; Debra	Willow Springs	IL		

US-CL-CURRENT: 514/284; 514/34, 514/80, 546/77, 546/78

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 6492427 B2

L4: Entry 6 of 29 File: USPT Dec 10, 2002

US-PAT-NO: 6492427
DOCUMENT-IDENTIFIER: US 6492427 B2

TITLE: Methods for treating multiple sclerosis

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shankar; L. Sai Latha	New York	NY	10128	
Tatton; William G.	Purchase	NY	10577	
Tatton; Nadine A.	Purchase	NY	10577	

US-CL-CURRENT: 514/646; 514/647, 514/654

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 6472432 B1

L4: Entry 7 of 29 File: USPT Oct 29, 2002

US-PAT-NO: 6472432
DOCUMENT-IDENTIFIER: US 6472432 B1

TITLE: Treatment of rosacea using lipoic acid

DATE-ISSUED: October 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/558; 514/440, 514/458, 514/557

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 6437004 B1

L4: Entry 8 of 29 File: USPT Aug 20, 2002

US-PAT-NO: 6437004
DOCUMENT-IDENTIFIER: US 6437004 B1

TITLE: Treatment of skin damage using olive oil polyphenols

DATE-ISSUED: August 20, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/738; 514/451, 514/452, 514/731

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 6429219 B1

L4: Entry 9 of 29 File: USPT Aug 6, 2002

US-PAT-NO: 6429219
DOCUMENT-IDENTIFIER: US 6429219 B1

TITLE: Treatment of chronic hypertension and related conditions with thiol complexes

DATE-ISSUED: August 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pearson; Don C.	Lakewood	WA		
Richardson; Kenneth T.	Anchorage	AK		

US-CL-CURRENT: 514/369; 514/494, 514/499, 514/578

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 10. Document ID: US 6410062 B1

L4: Entry 10 of 29 File: USPT Jun 25, 2002

US-PAT-NO: 6410062
DOCUMENT-IDENTIFIER: US 6410062 B1

TITLE: Method for the topical treatment and prevention of inflammatory disorders and related conditions using extracts of feverfew (Tanacetum parthenium)

DATE-ISSUED: June 25, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Callaghan; Theresa	Ax Delft			NL
Oddos; Thierry	Meudon			FR
Gendimenico; Gerard	Neshanic Station	NJ		
Martin; Katharine	Ringoes	NJ		

US-CL-CURRENT: 424/764; 424/725

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 11. Document ID: US 6365623 B1

L4: Entry 11 of 29 File: USPT Apr 2, 2002

US-PAT-NO: 6365623
DOCUMENT-IDENTIFIER: US 6365623 B1

TITLE: Treatment of acne using lipoic acid

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/448; 514/458, 514/724, 514/725

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 12. Document ID: US 6338855 B1

L4: Entry 12 of 29 File: USPT Jan 15, 2002

US-PAT-NO: 6338855
DOCUMENT-IDENTIFIER: US 6338855 B1

TITLE: Cleansing articles for skin and/or hair which also deposit skin care actives

DATE-ISSUED: January 15, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Albacarys; Lourdes Dessus	West Chester	OH		
McAtee; David Michael	Mason	OH		
Deckner; George Endel	Cincinnati	OH		

US-CL-CURRENT: 424/409; 424/402

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 13. Document ID: US 6319942 B1

L4: Entry 13 of 29 File: USPT Nov 20, 2001

US-PAT-NO: 6319942
DOCUMENT-IDENTIFIER: US 6319942 B1

TITLE: Topical scar treatments using alkanolamines

DATE-ISSUED: November 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/440; 514/561, 514/667

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 14. Document ID: US 6296861 B1

L4: Entry 14 of 29 File: USPT Oct 2, 2001

US-PAT-NO: 6296861
DOCUMENT-IDENTIFIER: US 6296861 B1

TITLE: Treatment of skin damage using conjugated linoleic acid and ascorbyl fatty acid esters

DATE-ISSUED: October 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 424/401; 514/557

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 15. Document ID: US 6291702 B1

L4: Entry 15 of 29 File: USPT Sep 18, 2001

US-PAT-NO: 6291702
DOCUMENT-IDENTIFIER: US 6291702 B1

TITLE: Azulenyl nitrone spin trapping agents, methods of making and using same

DATE-ISSUED: September 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Becker; David Alan	Ft. Lauderdale	FL		

US-CL-CURRENT: 560/51; 560/10, 560/35, 560/8, 562/11, 562/30, 562/427, 562/440, 562/462, 564/1, 564/123, 564/15, 564/253 , 564/257, 564/297, 564/298, 564/299, 564/300, 564/435, 564/440, 568/305, 568/423, 568/924, 568/949

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 16. Document ID: US 6242491 B1

L4: Entry 16 of 29 File: USPT Jun 5, 2001

US-PAT-NO: 6242491
DOCUMENT-IDENTIFIER: US 6242491 B1

TITLE: Use of creatine or creatine compounds for skin preservation

DATE-ISSUED: June 5, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kaddurah-Daouk; Rima	Belmont	MA	02178	

US-CL-CURRENT: 514/565

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 17. Document ID: US 6242010 B1

L4: Entry 17 of 29 File: USPT Jun 5, 2001

US-PAT-NO: 6242010
DOCUMENT-IDENTIFIER: US 6242010 B1

TITLE: Synergistic antioxidant compositions in management of hemorrhoids and other ano-rectal inflammatory conditions

DATE-ISSUED: June 5, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		

US-CL-CURRENT: 424/702; 424/400, 424/729, 424/94.1, 424/DIG.15, 514/562, 514/882, 514/937, 514/944, 514/966, 514/969

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 18. Document ID: US 6197825 B1

L4: Entry 18 of 29 File: USPT Mar 6, 2001

US-PAT-NO: 6197825
DOCUMENT-IDENTIFIER: US 6197825 B1

TITLE: Azulenyl nitrone spin trapping agents, methods of making and using same

DATE-ISSUED: March 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Becker; David Alan	Ft. Lauderdale	FL		

US-CL-CURRENT: 514/640; 514/114, 514/12, 514/21, 514/297, 514/510, 514/519, 514/553, 514/557, 514/561, 514/579, 514/613 , 514/644, 514/645, 514/676, 514/704, 514/740, 530/358, 530/387.1, 546/104, 546/106, 558/190, 558/303, 558/61, 560/35, 560/8, 562/11, 562/30, 564/1, 564/123, 564/15, 564/253, 564/257, 564/297, 564/298, 564/299, 564/300, 564/435, 564/440, 568/305, 568/423, 568/924, 568/929

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 19. Document ID: US 6191121 B1

L4: Entry 19 of 29 File: USPT Feb 20, 2001

US-PAT-NO: 6191121
DOCUMENT-IDENTIFIER: US 6191121 B1

TITLE: Treatment of skin damage using polyenylphosphatidylcholine

DATE-ISSUED: February 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/78; 424/400, 424/401

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 20. Document ID: US 6120756 A

L4: Entry 20 of 29 File: USPT Sep 19, 2000

US-PAT-NO: 6120756
DOCUMENT-IDENTIFIER: US 6120756 A

TITLE: Topical anionic salicylate for disorders of the skin

DATE-ISSUED: September 19, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Markowitz; Philip I.	Philadelphia	PA	19111	

US-CL-CURRENT: 424/70.1; 424/401, 424/59, 424/70.11, 514/844, 514/845, 514/846, 514/847, 514/887

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 21. Document ID: US 6087362 A

L4: Entry 21 of 29 File: USPT Jul 11, 2000

US-PAT-NO: 6087362
DOCUMENT-IDENTIFIER: US 6087362 A

TITLE: Apomorphine and sildenafil composition

DATE-ISSUED: July 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
El-Rashidy; Ragab	Deerfield	IL		

US-CL-CURRENT: 514/252.16; 514/284

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 22. Document ID: US 6080877 A

L4: Entry 22 of 29 File: USPT Jun 27, 2000

US-PAT-NO: 6080877
DOCUMENT-IDENTIFIER: US 6080877 A
**** See image for Certificate of Correction ****

TITLE: Taxanes

DATE-ISSUED: June 27, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Swindell; Charles S.	Merion	PA		
Shashoua; Victor E.	Brookline	MA		
Bradley; Matthews O.	Laytonsville	MD		
Webb; Nigel L.	Bryn Mawr	PA		

US-CL-CURRENT: 549/510; 549/511

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 23. Document ID: US 6048886 A

L4: Entry 23 of 29 File: USPT Apr 11, 2000

US-PAT-NO: 6048886
DOCUMENT-IDENTIFIER: US 6048886 A
**** See image for Certificate of Correction ****

TITLE: Compositions and delivery systems for the topical treatment of psoriasis and other conditions of the skin

DATE-ISSUED: April 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Neigut; Stanley	Plymouth Meeting	PA	19462	

US-CL-CURRENT: 514/412

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 24. Document ID: US 5965618 A

L4: Entry 24 of 29 File: USPT Oct 12, 1999

US-PAT-NO: 5965618
DOCUMENT-IDENTIFIER: US 5965618 A

TITLE: Treatment of scar tissue using lipoic acid

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perricone; Nicholas V.	Guilford	CT	06437	

US-CL-CURRENT: 514/558; 514/440

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 25. Document ID: US 5919815 A

L4: Entry 25 of 29 File: USPT Jul 6, 1999

US-PAT-NO: 5919815
DOCUMENT-IDENTIFIER: US 5919815 A

TITLE: Taxane compounds and compositions

. DATE-ISSUED: July 6, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bradley; Matthews O.	Laytonville	MD		
Shashoua; Victor E.	Brookline	MA		
Swindell; Charles S.	Merion	PA		
Webb; Nigel L.	Bryn Mawr	PA		

US-CL-CURRENT: 514/449; 549/510

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 26. Document ID: US 5906811 A

L4: Entry 26 of 29 File: USPT May 25, 1999

US-PAT-NO: 5906811
DOCUMENT-IDENTIFIER: US 5906811 A

TITLE: Intra-oral antioxidant preparations

DATE-ISSUED: May 25, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		

US-CL-CURRENT: 424/54; 424/49, 604/58

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 27. Document ID: US 5827886 A

L4: Entry 27 of 29 File: USPT Oct 27, 1998

US-PAT-NO: 5827886
DOCUMENT-IDENTIFIER: US 5827886 A

TITLE: Composition for relief of arthritis-induced symptoms

DATE-ISSUED: October 27, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		

US-CL-CURRENT: 514/562; 424/702, 514/162, 514/165, 514/171, 514/474, 514/561, 514/627

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 28. Document ID: US 5795909 A

L4: Entry 28 of 29 File: USPT Aug 18, 1998

US-PAT-NO: 5795909
DOCUMENT-IDENTIFIER: US 5795909 A

TITLE: DHA-pharmaceutical agent conjugates of taxanes

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shashoua; Victor E.	Brookline	MA		
Swindell; Charles S.	Merion	PA		
Webb; Nigel L.	Bryn Mawr	PA		
Bradley; Matthews O.	Laytonsville	MD		

US-CL-CURRENT: 514/449; 514/549

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 29. Document ID: US 5364884 A

L4: Entry 29 of 29 File: USPT Nov 15, 1994

US-PAT-NO: 5364884
DOCUMENT-IDENTIFIER: US 5364884 A
**** See image for Certificate of Correction ****

TITLE: Arginine compounds as ocular hypotensive agents

DATE-ISSUED: November 15, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Varma; Rajender S.	The Woodlands	TX		
Chiou; George C. Y.	College Station	TX		

US-CL-CURRENT: 514/551; 514/565, 514/616, 514/621, 514/913, 560/34

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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L4: Entry 29 of 29 File: USPT Nov 15, 1994

DOCUMENT-IDENTIFIER: US 5364884 A
**** See image for Certificate of Correction ****
TITLE: Arginine compounds as ocular hypotensive agents

Abstract Text (1):
The invention relates to arginine and arginine-like compounds and to methods employing these compounds as ocular hypotensive agents. These compounds are effective when applied topically, may be used in low concentrations and are nontoxic. Additionally, the invention includes several new arginine derivatives with varying lipophilicities particularly suited for topical administration.

Brief Summary Text (3):
The invention relates to novel arginine and arginine-like compounds, compositions for treating ocular hypertension and methods for prevention of retinal degeneration employing the compositions. The invention also includes methods for stimulating nitric oxide (NO) production and activation of guanylate cyclase.

Brief Summary Text (9):
There is thus a continued need for improved pharmaceutical compounds for treatment of ocular hypertension and glaucoma that may be administered topically or otherwise that will act effectively and selectively in reducing intraocular pressure without other pharmacological action or untoward side effects. Particularly desirable agents are those effective in low dosages and which lack toxicity.

Brief Summary Text (14):
Numerous other arginine compounds are considered suitable for the practice of the present invention. Considerations in selecting a suitable arginine compound will be based on the recognized difficulty of topically introducing compounds into the eye, due to factors such as absorption properties of the cornea and conjunctiva, tear turnover and solution drainage, recognizing that most ophthalmic preparations are administered as solutions. Therefore, one will desire to choose substituent groups that enhance the lipophilicity of the molecule with the objective of increasing the availability of the drug at the corneal surface and/or passage through the membrane. Likewise, one might also select "prodrug" compounds that will hydrolyze to arginine. For cleavage or hydrolysis one will wish to consider both the vehicle in which the compound is applied to the eye and also the potential of the ocular environment to cleave such compounds. For example, the aqueous humor of the eye may contain different esterases. Rabbit ocular tissues contain acetyl and butyrylcholinesterase (Lee and Li, 1989), with butyrylcholinesterase dominant, as it is in most ocular tissue. It is reported that lipophilic esters are hydrolyzed more readily than the hydrophilic esters, suggesting that hydrolysis and therefore availability may be increased by appropriate ester selection (Lee and Li, 1989). Lacrimal glands produce tears which do not generally contain esterases, although dilution and washing effects are a consideration in applying aqueous drug preparations directly to the eye.

Brief Summary Text (17):
Appropriate compounds for the practice of the present invention need not be limited to L-arginine and arginine derivatives. It is known that nitric oxide synthase converts L-arginine to NO (Bredt and Snyder, 1990). NO is involved in several important biological events including vascular smooth muscle relaxation, platelet deaggregation, neuronal communication and possible photoreceptor signaling, to

mention a few. NO involvement occurs through activation of guanylate cyclase, which is a heme containing enzyme catalyzing the reaction GTP.fwdarw.cGMP. Vasodilators such as nitroglycerin exert their pharmacological action by releasing nitric oxide. Thus, compounds that, like L-arginine, release NO in the presence of nitric oxide synthase will be expected to act like L-arginine as effective reducers of ocular hypertension. Generally, such compounds would contain amidine or amidoxime functions which could act as precursors of NO in vivo after oxidation by suitable enzymes in the presence of oxygen and NADPH. Aryl amidoximes would be particularly useful because of their increased lipophilic character.

Brief Summary Text (21):
Ophthalmic compositions intended to be administered topically will have a pH range from about 3 to about 9.5 and most preferably around pH 7.0-7.5 in order to avoid tissue irritation or damage. Any of numerous suitable non-toxic buffering agents may be employed including acetate, borate, carbonate, phosphate, citrate, Tris, etc. Compositions suitable for ocular administration are preferably in the form of emulsions, solutions, gels, aerosols or ointments. The preparation of such an ophthalmic composition would be generally known to those of skill in the art, as described, for example, in "Remington's Pharmaceutical Sciences" 15th Edition (Mack Publishing Co., Easton, Pa.).

Brief Summary Text (29):
Stabilizers such as chelating agents, for example EDTA, EGTA, DTPA, DOTA, ethylene diamine, bipyridine, 1,10-phenanthrolene, crown ethers, aza crown, catechols, dimercaprol, D-penicillamine and deferoxamine may be used. Antioxidants will also act as stabilizers and include such compounds as ascorbic acid, sodium bisulfite, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, potassium metabisulfite and sodium metabisulfite.

Brief Summary Text (34):
Typically used doses will generally be in the range of about 0.01% to 5% by weight, and usually about 0.1-0.5% when used topically. Frequency of treatment and dose level will, however, depend upon the severity of the condition and the nature of the disease being treated. Generally speaking, and in the cases of, for example, glaucoma, treatment will typically be from 3 to 4 times daily by topical administration.

Brief Summary Text (35):
Pharmaceutically acceptable compositions of arginine or arginine-related compounds may be applied topically to the ocular surface either alone or in combination with other drug delivery systems. Examples of such systems include hyaluronic acid solutions or suspensions of collagen fragments. The drugs may be formulated in microcapsules, designed with appropriate polymeric materials for controlled release, such as polylactic acid, ethylhydroxycellulose, polycaprolactone, polycaprolactone diol, polylysine, polyglycolic, polymaleic acid, poly[N-(2-hydroxypropyl)methylacrylamide] and the like. Particular formations may be in the form of liquid suspensions, ointments, complexes to a bandage, collagen shield or the like. In some cases, for example where there is existing damage to the cornea, the compositions may be administered intradermally or possibly subcutaneously.

Brief Summary Text (36):
The invention is therefore directed to compositions which include one or more arginine or arginine-related compounds in suitable pharmaceutical compositions that include pharmaceutically acceptable carriers. Ophthalmic solutions for topical administration for example would be administered to the eye of the subject in need of treatment in the form of an ophthalmic preparation prepared in accordance with conventional pharmaceutical practice, see for example Remington's Pharmaceutical Sciences, 15th Ed., pp. 1488-1501, Mac Publishing Co., Easton, Pa.

Detailed Description Text (2):
The enzyme nitric oxide synthase converts L-arginine to nitric oxide (NO) (Bredt and Snyder, 1990). The endogenously produced nitric oxide is also known as endothelium derived relaxation factor (EDRF) and has been implicated in the role of relaxing vascular smooth muscles. It is a potent stimulator of guanylate cyclase in several systems including retina (Venturini et al., 1991). Recently, however, it has been

suggested that S-nitrosothiols, but not free NO, are identical to EDRF rather than NO (Rubanyi et al., 1991). Additionally, the role of NO in physiological function is beginning to be elucidated, for example its role in vasodilation and platelet aggregation when combined with intracellular thiols (Radomski, et al., 1992; Myers, et al., 1990).

Detailed Description Text (3):
There is evidence of the presence of NO synthase in bovine retina (Venturini et al., 1991), activation of bovine rod outer segment guanylate cyclase by NO and the role of exogenous lipophilic activators or soluble guanylate cyclase in altering intraocular pressure. Thus, the discovery of L-arginine as a substrate for NO synthase prompted in vivo testing of this compound for reducing intraocular pressure. Surprisingly, the topical use of L-arginine and its lipophilic derivatives which are also substrates for the NO synthase, provide a convenient source of NO. NO is a potent vasodilator and modulator of guanylate cyclase thus making it an ideal compound for lowering intraocular pressure and for preventing and controlling retinal degeneration. L-arginine is a widely occurring, non-toxic natural amino acid.

Other Reference Publication (1):
Andronik-Lion et al., "Formation of Nitric Oxide by Cytochrome P450-Catalyzed Oxidation of Aromatic Amidoximes," Biochem. Biophys. Res. Commun., 185(1):452-458, 1992.

Other Reference Publication (3):
Bredt and Snyder, "Isolation of Nitric Oxide Synthetase, A Calmodulin-Requiring Enzyme," Proc. Natl. Acad. Sci. USA, 87:682-685, 1990.

Other Reference Publication (7):
Feelisch et al., "Thio;-Mediated Generation of Nitric Oxide Accounts for the Vasodilator Action of Furoxans," Biochem. Pharmacol., 44(6):1149-1157, 1992.

Other Reference Publication (8):
Feelisch, "The Biochemical Pathways of Nitric Oxide Formation from Nitrovasodilators: Appropriate Choice of Exogenous No Donors and Aspects of Preparation and Handling of Aqueous No Solutions," J. Cardiovasc. Pharmacol., 17(Suppl. 3):S25-S32, 1991.

Other Reference Publication (13):
Kilbourne et al., "Arginine Antagonists for Inhibition of Systemic Hypotension Associated with Nitric Oxide Production or Endothelialderived Relaxing Factor," Chem. Abstracts, CA Selects: Antitumor Agents, 26:15, Abstract #115:248105v, 1991, regarding PCT application WO 9109524.

Other Reference Publication (17):
Moncada et al., "Nitric Oxide: Physiology, Pathophysiology, and Pharmacology," Pharmacol. Rev., 43(2):109-142, 1991.

Other Reference Publication (18):
Myers, "Vasorelaxant Properties of the Endothelium-Derived Relaxing Factor More Closely Resemble S-Nitrosocysteine than Nitric Oxide," Nature, 345:161-162, 1990.

Other Reference Publication (24):
Robin et al., "Effects of Topical ALO 2145 (.rho.-Aminoclonidine Hydrochloride) on the Acute Intracular Pressure After Argon Laser Iridotomy," Arch. Ophthalmol., 105:1208-1211, 1987.

Other Reference Publication (25):
Rubanyl et al., "Evidence That a S-Nitrosothiol, but Not Nitric Oxide, May Be Identical with Endothelium-Derived Relaxing Factor," J. Cardiovasc. Pharmacol., 17(Suppl. 3):S41-S45, 1991.

Other Reference Publication (28):
Venturini et al., "Synthesis of Nitric Oxide in the Bovine Retina," Biochem. Biophys. Res. Commun., 180(2):920-925, 1991.

CLAIMS:

4. The method of claim 1 or claim 2 wherein said L-arginine ester derivative is administered topically to the eye in a pharmaceutically acceptable vehicle.

L4: Entry 27 of 29 File: USPT Oct 27, 1998

DOCUMENT-IDENTIFIER: US 5827886 A
TITLE: Composition for relief of arthritis-induced symptoms

Abstract Text (1):
A composition and method of using it for ameliorating inflammatory reactions and painful and other symptoms of the diseases of arthritis, lumbago, low back pain, myalgias and neuralgias. The composition includes reduced glutathione, a selenoamino acid and an anesthetic, such as capsaicin, in a suitable carrier for topical application.

Brief Summary Text (2):
The present invention deals with the combinations of several synergistic antioxidants, including enzymatic co-factors with analgesics such as capsaicin or the local caine anesthetics and anti-inflammatory agents in appropriate delivery vehicles employed in topical carriers as a means of ameliorating the inflammatory reactions and painful symptoms of a variety of arthritis syndromes, spinal pain, lumbago, myalgias and neuralgias and exercise and sport injuries. These clinical entities result primarily or secondarily from free radical damage to particular surfaces (joints and associated musculo-skeletal structures) resulting from a variety of inflammatory pathologies. A classic example is the process of "hypoxic-reperfusion injury" of rheumatoid arthritis where the etiologic factor is unknown but the free radical species and other products derived from the neutrophils "oxygen burst reaction" contribute to the joint's injury. All of these etiologies engender free radicals in joint spaces and contiguous cutaneous and musculo-skeletal tissues, requiring additional local antioxidant compositions to the therapeutic armamentarium of each disease state to aid in the amelioration of signs and symptoms and repair of the affected tissues. The synergistic locally applied antioxidants plus capsaicin as a depletor of substance P which is the major neuronal chemomediator of painful stimuli are thus adjuncts in the management of inflammation and pain in these clinical entities.

Brief Summary Text (4):
There are a number of rheumatologic and neurologic disorders as well as clinical musculo-skeletal syndromes where free radicals play a primary or secondary role in the clinical signs and symptoms of these distinct entities. Exercise, whether as calisthenics, weight lifting, swimming, running or jogging, generates free radical species. Exercise may be followed by muscle strain and aches or sprains, or result in painful sport injuries. The most common diseases affecting joints are rheumatoid arthritis and osteoarthritis. The former is an autoimmune disease where the articular inflammation in part leads to the generation of free radicals causing further inflammation and damage to the lining (synovium) of the affected joints. Free radicals also arise in rheumatoid arthritis and the other autoimmune related diseases, as periarteritis, lupus and scleroderma, through the mechanism of ischemia-reperfusion, similar to that in myocardial damage from coronary artery disease. The common syndromes of low back pain, fibrositis, and other neuro-muscular entities cause chronic pain from local inflammation. Thus, locally administered synergistic antioxidants play a role as adjuvant therapy alone or in combination with anti-inflammatory and analgesic medications, including topical capsaicin.

Brief Summary Text (8):
Another function of antioxidants is to catalytically convert the free radicals or other reactive oxygen species to a less reactive species. These body defenses may be

antioxidant enzymes while others are small molecule, non-enzymic antioxidants. Antioxidants are categorized by their activities as preventive or reparative antioxidants. The advantage of using these endogenous antioxidants in topical preparations is that the product provides locally the necessary and synergistically compatible antioxidants to exert a preventive, ameliorating or therapeutic function. In order to maintain normal cellular and tissue function and integrity of organ, there needs to be a local intracellular as well as extracellular balance between the generation of free radicals (reactive oxygen species) and corresponding enzymatic and non-enzymatic antioxidant defenses. When the balance shifts to a "net" increase in oxidant levels, cell damage ensues; conversely, when net levels of oxidants decrease, either through lower generation of reactive oxygen species and/or increases in antioxidant defenses, cellular integrity and function may be maintained.

Brief Summary Text (10):
Capsaicin, for topical medicinal purposes, is obtained from the dried fruits of the botanical family of capsicum, particularly C. frutescens L. and C. annum L., in conformance with applicable standards of the federal Food, Drug, and Cosmetic Act. Capsaicins are commercially available for cosmetics by suppliers such as Kalsec Inc. of Kalamazoo, Mich. Because the capsaicinoids are extremely pungent and irritating in high concentrations, MSDS should be obtained and precautions observed during their preparation. Use of capsaicin is restricted to a range of 0.025% to 0.075% by weight.

Brief Summary Text (11):
A number of clinical studies have been reported on the beneficial effects of capsaicin in the various diseases and syndromes herein mentioned. Recent reviews of the clinical applications of capsaicin as an adjuvant analgesic in pain management have been reported. In dealing with arthritis, researchers have reported a significant reduction of the severity of knee pain in patients with both osteoarthritis and rheumatoid arthritis treated with topically applied 0.025% capsaicin. Another study showed significant reduction of pain and tenderness of the hands with capsaicin 0.075% only in patients with osteoarthritis. In other studies in rheumatoid patients, topical capsaicin has caused greater reductions of synovial fluid inflammatory mediators, such as substance IL-6 and prostaglandin E, during and after topical treatment than using control vehicle cream. Researchers have editorialized that capsaicin exerts an anti-inflammatory reaction by enhancing migration of phagocytes without the generation of superoxide anion and by reducing neurogenic inflammation. When capsaicin is chronically administered, it enhances chemotaxis and increases collagenase production.

Brief Summary Text (16):
In disease states in humans, there is usually increased formation of free radicals, that is, reactive oxygen species which occur secondary to the etiologic disease process, but also contributory to local injury (examples: lung damage in adult respiratory distress syndrome and joints in rheumatoid arthritis). Oxygen free radicals attack cell structures, are cytotoxic and have been implicated in the pathogenesis of various disease states. Reactive oxygen species are generated continuously in vivo at chronically inflamed sites, such as the human joint in various arthritides, such as rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis and others. The arthritic joint as a site of oxidative stress, an overproduction of free radicals, exceeds the inherent, local antioxidant capacity thereby causing damage. Enhanced anti-inflammatory and antioxidant support may be provided by oral, parenteral or local topical compositions as described herein. These result, as stated, in reduction of free radicals and their damage by the scavengers as well as reduction of the inflammatory synovial response. The complex cascades that comprise the inflammatory reaction occur primarily to limit tissue damage and prevent or inhibit infections.

Brief Summary Text (33):
As previously noted, the present invention deals with glutathione (GSH) in combination with selenium and thiol compounds such as those containing glutathione reductase and sulphur amino acids plus other synergistic antioxidants used topically to act as free radical scavengers and neutralizers reducing inflammatory reactions in various clinical rheumatologic and musculo-skeletal entities and analgesics, such as capsaicin to diminish pain. It is proposed that the described active ingredients be

employed in topical compositions. Topical carriers are employed which should be both non-irritating to the skin and which are suitable for delivering the active components to the affected areas. Further, suitable topical carriers should be those which do not inhibit the antioxidant activity of the active ingredients thus reducing the efficiency of the composition. Further, such carriers must be of sufficiently high purity and sufficiently low toxicity to render them suitable for chronic topical administration to the skin and be free of bacterial contaminants.

Brief Summary Text (34):
The topical use of anti-inflammatory agents to reduce and alleviate swelling and erythema of inflammatory lesions and the associated pain syndrome has been well established. Many topical preparations are on the market, but mainly as anti-inflammatory creams, lotions, ointments or gels. These compositions ordinarily contain steroidal anti-inflammatories, non-steroidal (salicylates and nsaids) and natural anti-inflammatories, such as extract of aloe vera. Thus, in association with the present anti-oxidants, the anti-inflammatories are incorporated to provide topical preparations in stable forms to ameliorate the inflammatory reaction as is well known in the therapeutic art of the clinical conditions. In addition, anti-inflammatories are used in these topical preparations to reduce local inflammatory reactions and pain of the various types of arthritis, myalgias, neuralgias, lumbago, low back pain and associated dermatoses of diverse various etiologies. Symptomatic relief is afforded in addition to the specific therapies for each of these entities.

Brief Summary Text (35):
Inflammatory lesions have pathologic responses which include the presence of neutrophils (leukocytes). Systemic leukocytosis may be a reflection of infection or other generalized disorders. Immunological defense mechanisms are also called into play in these inflammatory reactions. Liberation of free radicals during these inflammatory lesions of various etiologies are also accompanied by the so-called "oxidative burst" of activated neutrophils. This "oxidative burst" produces abundant superoxide radical, which is believed to be an essential factor in producing the cytotoxic effect of activated neutrophils. Providing the antioxidants in topical preparations with combinations of anti-inflammatory agents to have a wide spectrum therapeutic effect on these dermatologic, neuro-muscular, vascular and articular pathologies is an important aspect of the present invention.

Brief Summary Text (42):
Ascorbic acid can be employed in these compositions in an amount between 0.01% to 25% by weight based upon the weight of the active ingredients, preferably from 0.1% to 10% by weight, most preferably from 1.0% to 3% by weight. Most preferably, the ascorbic acid to be used in these compositions will be protected by encapsulation, such as liposomes or nanospheres as is well known in the art by chemical bonding such as in ascorbyl palmitate or ascorbyl glucosamine. Ascorbyl glucosamine would be used in a range of 0.05% to 12% by weight based on the weight of the active ingredients, preferably from 0.5% to 9% by weight and most preferably from 1.5% to 7.5% by weight.

Brief Summary Text (43):
Thus, these topical preparations will, in their preferred form, contain mixtures of vitamins C and E to enhance locally the anti-oxidant activities of the active ingredients, particularly in their function as chain-breaking anti-oxidants in lipid peroxidation.

Brief Summary Text (45):
Beta-carotene, which is pro-vitamin A, is found in many plants and is a nutrition source and the main coloring matter in carrots and egg yolks. B-carotene is used in cosmetics as a coloring agent and also as a source to the body of vitamin A. Carotene, like vitamin A compounds, may be absorbed by the skin. Carotenoids, including beta-carotene, are small molecule dietary and topical anti-oxidants. Carrot oil is rich in vitamin A and carotenoids and may be used in these preparations in a concentration of at least 0.001% to 1.0% as a source of these molecules. It is a light yellow essential oil derived from seeds of carrots and has no known toxicity. Carrot seed extract, may also be used and is derived from the seed of Daucus carota sativa.

Brief Summary Text (46):
Wahl and co-workers at the National Institutes of Health taught methods to treat chronic inflammatory diseases including the various arthritis syndromes in U.S. Pat. No. 5,499,688 issued Sep. 12, 1995, which is herein incorporated by reference. They administered effective amounts of nitric oxide scavengers to decrease the amount of putative nitric oxide present at the site of the inflammation. These compounds belonged to complexes with L-arginine, L-canavanine, citrulline and aminoguanidine. They note, akin to the argument herein, favoring the use of antioxidants to neutralize free radicals. This '688 patent augurs a method for suppressing joint disease, inflammation, tissue swelling and bone and cartilage degradation in chronic arthritis.

Brief Summary Text (47):
Certain antioxidants, particularly the endogenous L-glutathione and superoxide dismutase, as well as the element selenium, a co-factor for the enzyme glutathione peroxidase, and thiol compounds such as L-cysteine, can be employed in suitable carriers such as lotions, solutions, creams, ointments, foundation products, balms, sprays, aerosols or gels to protect and to treat the overlying skin surface in dealing specifically with the effects of the various free radicals on biomolecules, lipids and cell membranes. Moreover, anti-inflammatory agents, topical anesthetics, and pain reliever ingredient capsaicin in appropriate concentration and delivery vehicles are to be incorporated within these free radical scavenger and pain relief preparations.

Brief Summary Text (57):
Of interest herein, acetyl L-carnitine has been shown to have a scavenging effect on the free superoxide anion. This antioxidant activity coupled by acetyl L-carnitine's effect of inducing an increase in reduced glutathione and reduced ubiquinone levels provides a stabilizing effect on membranes by decreasing membrane lipid peroxidation. Acetyl-L-carnitine is optionally employed in these compositions in dosages of at least approximately 0.001% to 5% by weight and most preferably from 0.1% to 1.0% by weight. Thus, reduced glutathione and acetyl L-carnitine in topical preparations will act somewhat synergistically; the former as an antioxidant which itself becomes oxidized and better able to be regenerated locally in its reduced form by the metabolic functions of acetyl L-carnitine.

Brief Summary Text (58):
Further, glutathione and selenium act synergistically in vivo as they are both constituents of the same enzymatic system. GSH serves as a specific donor substrate while selenium, provided from alimentary sources or locally from topically applied preparations of selenoamino acids, as herein mentioned, or selenium yeast extracts provide the prosthetic group of GSH peroxidase, during its synthesis. The glutathione and selenium antioxidant functions are intrinsically related since by keeping a peroxidase in action, the GSH and selenium contribute to the removal of the dismutation product of free oxygen radicals, namely, hydrogen peroxide. In a broad sense, GSH and selenium modulate free radical chains initiated or sustained by hydroperoxides.

Brief Summary Text (63):
As noted previously, the active ingredients described above can be incorporated in any suitable pharmacologically acceptable carrier which is suitable for topical administration to the human skin. As such, the pharmacologically acceptable carrier must be of sufficient purity and have sufficiently low toxicity to render it suitable for administration to a human. The carrier may represent a major portion of the total composition from at least approximately 80%.

Brief Summary Text (65):
Solvents are generally employed in the preparation of suitable topical compositions. Such solvents can either be aqueous or organic based and, in either case, the solvent must be capable of having dispersed or dissolved therein the above-described active components while not being irritating to the user. Water is a typical aqueous solvent while suitable organic solvents include propylene glycol, butylene glycol, polyethylene glycol, polypropylene glycol, glycerol, 1,2,4-butanetriol, sorbitol esters, 1,2,6-hexanetriol, ethanol, isopropanol, butanediol and mixtures thereof.

Solvents can be included in the overall composition in amounts ranging from 0.1% to 99% and preferably from 2.0% to 75%. It is noted that compositions of the present invention can be produced in the form of an emollient. A wide variety of suitable emollients are known and may be used herein. In this regard, reference is made to U.S. Pat. No. 5,296,500, the disclosure of which is incorporated by reference.

Brief Summary Text (72):
It is also contemplated that, as a further optional expedient that the present composition optimally contain from approximately 0.01% to 10% Japanese green tea. Chemically, extracts of Japanese green tea have been analyzed and characterized. Active ingredients include caffeine, theobromine, theophylline and xanthines which, together, have been shown to reduce irritation. Green tea also contains potent polyphenols, catechin compounds, which effectively act as antioxidant agents to scavenge for radicals. The main catechin constituent of green tea is (--)epigallo catechin gallate (EGCG). It has also been shown that EGCG inhibits hydrogen peroxide formation by human leukocytes, the first cell in the inflammatory cellular response to injury. EGCG is of value to function synergistically as an exogenous antioxidant in these topical preparations with the active ingredients comprised of endogenous antioxidants.

Detailed Description Text (2):
The following formulation is directed to the making of a cream for topical application employing the active ingredients of the present invention.

Detailed Description Text (4):
The following formulation is directed to the making of a lotion for topical application employing the active ingredients of the present invention.

Detailed Description Text (10):
Salicylic acid and its derivatives are inhibitors to the prostaglandins and thus lessen inflammatory reactions. Topical preparations can be used to reduce local skin inflammation as well as alleviating inflammation in incidents of trauma and various other conditions associated with free radicals and inflammation such as disorders of joints, bursa, muscles and tendons.

Detailed Description Text (11):
The aforementioned is a prototype example of an ointment with the synergistic antioxidant complex to fight free radicals. This composition can also be made with the addition of capsaicin 0.025% to 0.075% to reduce the pain mediator, substance P, and/or with the addition of local anesthetics of the caine family, such as benzocaine in percents ranging from 0.10% to 5.0%, most preferably from 0.5 to 1.0. Reller and Kretschmar taught the use of analgesic and anti-inflammatory compositions, particularly salicylic acid for topical applications in U.S. Pat. No. 4,199,576, (Apr. 22, 1980), which is herein incorporated by reference. Also included herein by reference is U.S. Pat. No. 5,612,321 (Lin and Baier - Mar. 18, 1997) which teaches that panthotenic acid in combinations with salicylic acid renders the topical compositions less irritating to the skin.

Detailed Description Text (18):
In addition to the antioxidant complex disclosed herein, the gel may contain menthol in concentrations of 0.01% to 0.1% or steroids, like hydrocortisone in concentrations from approximately 0.01 to 1.0% or anti-inflammatories such as ibuprofen, indomethacin, sulindac and naproxen in effective, safe and therapeutic amounts as established in pharmaceutical preparations well known in this industry. Although ethanols may be used in topical gel compositions, these preparations may optionally be made without alcohol and contain standard gelling compounds together with the antioxidant complex. Such an example would also be prepared by combining standard components utilizing usual conventional mixing formulations and techniques. Salicylates, steroidal salicylates and non-steroidal anti-inflammatory agents may be optional ingredients in the compositions of this invention as are well known in the art. Many of these well known anti-inflammatories are enumerated in various patents, including U.S. Pat. No. 5,384,115 by Bissett and co-workers (Jan. 24, 1995) which is herein incorporated by reference.

Detailed Description Paragraph Table (4):

SALYCYLIC ACID OINTMENT WITH ANTIOXIDANT COMPLEX Ingredient Percent By Weight cetyl alcohol balance oleyl alcohol 30.0 propylene glycol 25.0 Germaben II 1.0 salicylic acid 3.0 L-glutathione 0.10 L-selenomethionine 0.10 superoxide dismutase 0.20 ascorbyl palmitate 2.00 tocopheryl acetate 1.00 carrot oil 0.20 green tea 0.50 dex panthenol 0.75

Detailed Description Paragraph Table (5):

Ingredients Percent By Weight L-glutathione 0.1 selenomethionine 0.05 ascorbyl palmitate 1.5 tocopherol acetate 1.0 superoxide dismutase 0.1 acetyl-L-carnitine 0.03 capsaicin 0.025

CLAIMS:

1. A topical composition for ameliorating inflammatory reactions and symptoms of the various diseases and syndromes of arthritis, lumbago, myalgias and neuralgias and post-exercise symptoms and low back pain syndrome comprising reduced glutathione, a selenoamino acid and an anesthetic in suitable quantities to reduce inflammation and chronic pain characteristic of said diseases in a suitable carrier for topical application.

11. A method of ameliorating inflammatory reactions and symptoms of the diseases of arthritis, lumbago, low back pain, myalgias and neuralgias and post-exercise syndromes comprising topically applying active ingredients in a suitable topical carrier to an area of the body in which said symptoms are manifested, said active ingredients comprising reduced glutathione, a selenoamino acid and an anesthetic in suitable quantities to reduce inflammation and chronic pain characteristic of said disease.

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L4: Entry 24 of 29 File: USPT Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5965618 A
TITLE: Treatment of scar tissue using lipoic acid

Abstract Text (1):
Scar tissue is reduced or inhibited by application of a composition containing lipoic acid and/or a lipoic acid derivative such as dihydrolipoic acid, a lipoic or dihydrolipoic acid ester, a lipoic or dihydrolipoic acid amide, a lipoic or dihydrolipoic acid salt, and mixtures of any of these. Some compositions further comprise .alpha.-hydroxy acids or acid derivatives such as glycolic and/or lactic acid, fatty acid esters of ascorbic acid such as ascorbyl palmitate, and/or tocotrienol. In some embodiments, a silicone gel sheet with added lipoic acid and/or a lipoic acid derivative and optional other ingredients is topically applied to scar tissue to diminish them.

Brief Summary Text (10):
Formation of scars, especially hypertrophoic and keloid scars, is dependent on systemic growth factors such as interleukins and other cytokines, and their influence on fibronectin and collagen biosynthesis. Cytokines are released and are present in the wound healing process and sometimes are released in the inflammatory stage. Growth factors and other cytokines vary in the inflammatory stage and are released based, among other complex interactions, upon the redox state of the cells. The presence of free radicals in the inflammatory stage plays an important factor in wound healing. Factors that increase the presence of free radicals, such as infection, radiation, and continued trauma, may instigate hypertrophic and keloid scar formation. It is important to note that cytokines have been suggested to regulate nitric oxide synthetase, which controls the formation of nitric oxide, which plays an important role in signal transduction in the cells. It has also been suggested that nitric oxide synthetase activity is aberrant in keloid scars when compared to normal scar tissue (Lim, T. C., et al., Plastic and Reconst. Surgery, 1996, 98:911-912). Hypertrophic and keloid scars also show inflammatory activity that is not seen in mature scars.

Brief Summary Text (11):
Many scar treatments have been suggested, but few are satisfactory. Treatment of keloid or hypertrophic scars have consisted of surgical excision followed in many cases by graft application. Pressure has also been used to cause scar thinning after injury or scarring. For example, pressure bandages placed over scars have resulted in some scar thinning, but a pressure of at least about 25 mm Hg must be maintained constantly for approximately six months in usual situations for any visually observable effect. Ionizing radiation therapy has also been employed. Other treatments include application of silicone pads to the scar tissue surface, sometimes under pressure provided by an elastomeric bandage, application of silicone gel sheets, with or without added vitamin E (Palmieri, B., et al., J. Derm., 1995, 34: 506-509), and topical or intralesional treatment with corticosteroids.

Brief Summary Text (15):
It is another and more specific objective of the invention to provide topical compositions and methods for scar reduction and inhibition based upon topical application of compositions containing lipoic acid and/or lipoic acid derivatives, typically in association with a dermatologically acceptable carrier or vehicle and/or a silicone gel sheet, to scars and to injured skin sites susceptible to scarring.

Brief Summary Text (16):
These and other objectives are accomplished by the present invention, which provides compositions and methods for the treatment and/or inhibition of cutaneous scars, which comprises topical application to the scars or injured skin areas of an effective amount of lipoic acid, lipoic acid derivatives or mixtures thereof. Some embodiments employ compositions containing lipoic acid and/or a lipoic acid derivative in a dermatologically acceptable carrier which is applied to diminish or inhibit scar tissue. Others utilize a silicone gel sheet having added lipoic acid and/or a lipoic acid derivative which is applied to scar tissue.

Brief Summary Text (17):
Ascorbic acid, particularly fat-soluble fatty acid esters of ascorbic acid such as ascorbyl palmitate, can, optionally, also be utilized for further enhancing the efficacy of the therapeutic or prophylactic treatment. In other embodiments, tocotrienols or derivatives thereof or vitamin E compositions enriched with tocotrienols or tocotrienol derivatives such as tocotrienol-enriched fractions of natural oils are included in the lipoic acid composition with or without an ascorbic acid ingredient. Still other embodiments include .alpha.-hydroxy acids or their derivatives and the like in the lipoic acid composition with or without other optional ingredients.

Brief Summary Text (18):
In a preferred practice of the invention, the lipoic acid (or derivative) is applied in admixture with a dermatologically acceptable carrier or vehicle (e.g., as a lotion, cream, ointment, soap, or the like) so as to facilitate topical application and, in some cases, provide additional therapeutic effects as might be brought about, e.g., by moisturizing of the affected skin areas. As noted, other ingredients, particularly ascorbyl palmitate and/or tocotrienol and/or an .alpha.-hydroxy acid, can be advantageously included in the compositions. In one preferred embodiment, a silicone gel sheet having added lipoic acid and/or dihydrolipoic acid and/or other optional ingredients is applied to scar tissue or injured cutaneous sites susceptible to scarring.

Brief Summary Text (26):
However, only effective amounts of lipoic acid are needed to reduce or inhibit scar tissue, so generally topical application to exposed or affected skin sites is accomplished in association with a carrier, and particularly one in which the active ingredient is soluble per se or is effectively solubilized (e.g., as an emulsion or microemulsion) or available when applied in a silicone gel sheet or other linament. Where employed, the carrier is inert in the sense of not bringing about a deactivation of the lipoic acid or derivative, and in the sense of not bringing about any adverse effect on the skin areas to which it is applied.

Brief Summary Text (28):
While the carrier for lipoic acid can consist of a relatively simple solvent or dispersant, it is generally preferred that the carrier comprise a composition more conducive to topical application, and particularly one which will form a film or layer on the skin to which it is applied so as to localize the application and provide some resistance to perspiration and/or one which aids in percutaneous delivery and penetration of the active ingredients into lipid layers of the scarred area. Many such compositions are known in the art, and can take the form of lotions, creams, gels or even solid compositions (e.g., stick-form preparations). Typical compositions include lotions containing water and/or alcohols and emollients such as hydrocarbon oils and waxes, silicone oils, hyaluronic acid, vegetable, animal or marine fats or oils, glyceride derivatives, fatty acids or fatty acid esters or alcohols or alcohol ethers, lanolin and derivatives, polyhydric alcohols or esters, wax esters, sterols, phospholipids and the like, and generally also emulsifiers (nonionic, cationic or anionic), although some of the emollients inherently possess emulsifying properties. These same general ingredients can be formulated into a cream rather than a lotion, or into gels, or into solid sticks by utilization of different proportions of the ingredients and/or by inclusion of thickening agents such as gums or other forms of hydrophilic colloids. Such compositions are referred to herein as dermatologically acceptable carriers. Most preferred for skin are those carriers which are fat-soluble, i.e., those which can effectively penetrate skin layers and deliver LA to all skin layers.

Brief Summary Text (30):
As summarized above, many preferred embodiments of this invention contain at least one other ingredient in addition to lipoic acid. For example, fat-soluble fatty acid esters of ascorbic acid (vitamin C) may be added to the lipoic acid composition in some embodiments. The more oxidation-resistant saturated fatty acid esters of ascorbic acid are preferred, including, but not limited to, ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, and ascorbyl behenate. Ascorbyl palmitate is used in one embodiment. As denoted herein, where fatty acid esters are described, e.g., ascorbyl stearate, compositions having predominantly that ester, e.g., predominantly stearate, are included. The esters may be prepared using hydrogenated oils or fats, or fractions thereof, and contain small amounts of another ester. Ascorbyl stearate prepared using canola, for example, commonly contain about 4% ascorbyl palmitate.

Brief Summary Text (37):
While not wishing to be bound to any theory, it is possible that lipoic acid is efficacious in the treatment of scar tissue because it is fat- and watersoluble and readily disperses in cell membranes and other cellular components. It acts as a free radical scavenger and neutralizer, and prevents the cross-linking of cell membranes that is seen in scar formation, particularly keloid scar formation. By the same token, LA modulation of free radicals and other oxidative species affects gene expression, including expression of nuclear factor .kappa.-B (NF-.kappa.B), nitric oxide synthetase and other mediators at all stages of proinflammation and inflammation. Lipoic acid's alteration of lipid peroxidation, protein cross-linking, growth factor stimulation, and membrane permability may explain its negative effect on scar tissue formation.

Brief Summary Text (38):
The method of the present invention is particularly useful for reducing or inhibiting scars caused by minor lacerations, surgical wounds, vaccines, burns, and abrasions, as well as stretch marks observed in aging and after weight loss or childbirth and various types of fibroses. Generally, the composition is topically applied to the affected skin areas in a predetermined or as-needed regimen either at intervals by application of a lotion or the like, or continuously using a silicone gel sheet, it generally being the case that gradual improvement is noted with each successive application. Insofar as has been determined based upon clinical studies to date, no adverse side effects are encountered.

Detailed Description Text (4):
A second study was made on five subjects aged 18 to 30 years having striae distensae. Compositions containing 3% lipoic acid, a 1% tocotrienol-rich palm oil fraction, and 1% ascorbyl palmitate were applied to the striae twice daily for two months. At the end of that period, two of the subjects exhibited an 80% reduction in striae, while the remainder showed a 50% reduction in striae.

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☐ 1. Document ID: US 6528521 B2

L6: Entry 1 of 10 File: USPT Mar 4, 2003

US-PAT-NO: 6528521
DOCUMENT-IDENTIFIER: US 6528521 B2

TITLE: Treatment of anti-depression drug-induced sexual dysfunction with apomorphine

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

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Perdok; Renee J.	Gurnee	IL		

US-CL-CURRENT: 514/284

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. Desc | Image

☐ 2. Document ID: US 6506765 B2

L6: Entry 2 of 10 File: USPT Jan 14, 2003

US-PAT-NO: 6506765
DOCUMENT-IDENTIFIER: US 6506765 B2

TITLE: Apomorphine derivatives and methods for their use

DATE-ISSUED: January 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gupta; Pramod K.	Gurnee	IL		
Milkowski; Deborah	Chicago	IL		
Sutkowski-Markmann; Debra	Willow Springs	IL		

US-CL-CURRENT: 514/284; 514/34, 514/80, 546/77, 546/78

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. Desc | Image

☐ 3. Document ID: US 6248363 B1

L6: Entry 3 of 10 File: USPT Jun 19, 2001

US-PAT-NO: 6248363
DOCUMENT-IDENTIFIER: US 6248363 B1

TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions

DATE-ISSUED: June 19, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Patel; Mahesh V.	Salt Lake City	UT		
Chen; Feng-Jing	Salt Lake City	UT		

US-CL-CURRENT: 424/497; 424/422, 424/427, 424/430, 424/433, 424/434, 424/435, 424/436, 424/441, 424/451, 424/457, 424/463, 424/464, 424/465, 424/466, 424/470, 424/474, 424/476, 424/482, 424/489, 424/490, 424/498, 514/772.3, 514/773, 514/779, 514/784, 514/785, 514/786

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 4. Document ID: US 6087362 A

L6: Entry 4 of 10 File: USPT Jul 11, 2000

US-PAT-NO: 6087362
DOCUMENT-IDENTIFIER: US 6087362 A

TITLE: Apomorphine and sildenafil composition

DATE-ISSUED: July 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
El-Rashidy; Ragab	Deerfield	IL		

US-CL-CURRENT: 514/252.16; 514/284

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 5993851 A

L6: Entry 5 of 10 File: USPT Nov 30, 1999

US-PAT-NO: 5993851
DOCUMENT-IDENTIFIER: US 5993851 A

TITLE: Method for preparing biphasic multilamellar lipid vesicles

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foldvari; Marianna	Saskatoon			CA

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.32, 264/4.6, 424/1.21, 424/417, 424/85.7, 424/9.321, 424/9.51

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 5888534 A

L6: Entry 6 of 10 File: USPT Mar 30, 1999

US-PAT-NO: 5888534
DOCUMENT-IDENTIFIER: US 5888534 A

TITLE: Controlled release of drugs delivered by sublingual or buccal administration

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
El-Rashidy; Ragab	Deerfield	IL		
Ronsen; Bruce	River Forest	IL		
Hassan; Emad Eldin	Alexandria			EG

US-CL-CURRENT: 424/435; 424/464, 424/465, 424/468, 424/473, 514/770, 514/772.1, 514/772.2, 514/772.3, 514/774, 514/777, 514/778, 514/779, 514/781, 514/782

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 5853755 A

L6: Entry 7 of 10 File: USPT Dec 29, 1998

US-PAT-NO: 5853755
DOCUMENT-IDENTIFIER: US 5853755 A

TITLE: Biphasic multilamellar lipid vesicles

DATE-ISSUED: December 29, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foldvari; Marianna	Saskatoon			CA

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.32, 264/4.6, 424/1.21, 424/417, 424/9.321, 424/9.51, 428/402.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 8. Document ID: US 5633276 A

L6: Entry 8 of 10 File: USPT May 27, 1997

US-PAT-NO: 5633276
DOCUMENT-IDENTIFIER: US 5633276 A

TITLE: Indoline derivatives, method of preparation and use

DATE-ISSUED: May 27, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
North; Peter C.	Stevenage			GB
Carter; Malcolm C.	Stevenage			GB

US-CL-CURRENT: 514/411; 548/430

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 5624677 A

L6: Entry 9 of 10 File: USPT Apr 29, 1997

US-PAT-NO: 5624677
DOCUMENT-IDENTIFIER: US 5624677 A

TITLE: Controlled release of drugs delivered by sublingual or buccal administration

DATE-ISSUED: April 29, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
El-Rashidy; Ragab	Deerfield	IL		
Ronsen; Bruce	River Forest	IL		
Hassan; Emad E.	Sidi Gaber			EG

US-CL-CURRENT: 424/435; 424/464, 424/465, 424/468, 424/473, 514/770, 514/772.2, 514/772.3, 514/774, 514/778, 514/779, 514/781

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 10. Document ID: US 5565466 A

L6: Entry 10 of 10 File: USPT Oct 15, 1996

US-PAT-NO: 5565466
DOCUMENT-IDENTIFIER: US 5565466 A
**** See image for Certificate of Correction ****

TITLE: Methods for modulating the human sexual response

DATE-ISSUED: October 15, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gioco; Diane-Marie	West Haven	CT		
Zorgniotti, deceased; Adrian	late of Wyland	MA		

US-CL-CURRENT: 514/280; 514/212.01, 514/307, 514/396, 514/400, 514/471, 514/509, 514/523, 514/532, 514/644, 514/649

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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Terms	Documents
L1 and erectile	10

Display Format: - Change Format

Previous Page Next Page

L6: Entry 7 of 10 File: USPT Dec 29, 1998

DOCUMENT-IDENTIFIER: US 5853755 A
TITLE: Biphasic multilamellar lipid vesicles

Brief Summary Text (11):
Numerous agents have been employed in the therapy of impotence. Hormonal manipulation, such as replacement androgen therapy, has been used. However, patients with organic impotence are rarely candidates for hormonal manipulation. Thus, this mode of therapy should be strictly limited to cases in which endocrine deficiencies are established. Furthermore, in about 50 percent of patients with an endocrinopathy, a psychogenic etiology can be shown to be the predominant factor in erectile difficulties. Therefore, in the vast majority of impotent men, vascular and neurologic factors are the underlying causes. The most commonly used treatment for these patients is the implantation of penile prostheses. The invasive nature of this technique, coupled with the increasing evidence of mechanical failure, surgical complications, or infection has again focused attention on the development of pharmacological agents with a potential for improving the libido and quality of erections. Several agents have been tested e.g. bromocriptine, glyceryl trinitrate, zinc, oxytocin, yohimbine and nitroglycerin. Intracorporeal injection of vasoactive agents is now considered the treatment of choice for many patients with organic impotence (Kattan et. al., 1991).

Brief Summary Text (12):
Injection of papaverine, a smooth muscle relaxant, or a combination of papaverine and phentolamine (an a-adrenergic blocker) directly into the corpus cavernosum (either of the two erectile columns of the dorsum of the penis) has been shown to be an effective therapy in impotence. Recently, intercavernosal injections of prostaglandin E.sub.1 (alprostadil), a naturally occurring chemical derived from dihomo-gammalinolenic acid (20:3.infin.6) was discovered to also induce erection.

Brief Summary Text (13):
Injection of prostaglandin E.sub.1 results in vasodilation, with increased arterial inflow and decreased venous outflow by occlusion of draining venules, probably through relaxation of corporal smooth muscle. Due to its potent relaxant effect on vascular smooth muscle, prostaglandin E.sub.1 is used to maintain the patency of the ductus arteriosus in the neonate. This is the only currently approved (FDA) indication for prostaglandin E.sub.1. The effect of prostaglandin E.sub.1 on erectile dysfunction is known to be dose dependent.

Brief Summary Text (45):
Also within the scope of the invention is a method for the treatment of erectile dysfunction. This method comprises topically administering to a patient in need thereof an effective amount of a liposome composition comprising a population of multilamellar lipid vesicles having a prostaglandin, preferably PGE.sub.1, entrapped within the vesicles.

Detailed Description Text (4):
Separately there is prepared an anhydrous proliposome gel by admixing the phospholipid, glycolipid or ceramide and a pharmaceutically acceptable hydrophilic solvent, preferably propylene glycol, and heating them to form a melt. In the melt there may also be incorporated a material to enhance the strength of the lipid bilayers, for example cholesterol, a material to enhance penetration, for example monolauroyllysine and a material to impart a charge to the lipid bilayers, for

example stearic acid. A small amount of an antioxidant, for example ascorbyl palmitate, can be incorporated in the melt. The aqueous emulsion is added to the melt and the various components are subjected to gentle agitation which results in formation of the desired multilamellar lipid vesicles having in the central core compartment an aqueous emulsion containing the oil and consistency enhancer as the dispersed phase. A water-soluble biologically active material can be incorporated in solution in the aqueous phase of the emulsion. An oil-soluble biologically active material can be dissolved in the oil, before the emulsion is prepared, and incorporated into the vesicles in the emulsified oil droplets. Additionally or alternatively, an oil-soluble or solid or semi-solid biologically active material can be included in the anhydrous proliposome gel and incorporated into the vesicles in the lipid bilayers.

Detailed Description Text (48):
Encapsulation of PGE.sub.1 into multilamellar lipid vesicles for the preparation of liposome composition used in the treatment of erectile dysfunctions

Detailed Description Paragraph Table (5):

	% (w/w)
A. COMPOSITIONS FREE OF BIOLOGICALLY ACTIVE MATERIAL BUT SUITABLE FOR USE AS A VEHICLE FOR ADMINISTRATION OF SUCH A MATERIAL	
1. Topical liposomal product with encapsulated oil droplet Proliposome gel: Phospholipon 90H	5.0
Cholesterol	2.0
Stearic acid	1.0
Propylene glycol	7.0
Emulsion: Part 1: Distilled water q.s. to	100
PEFA	4.0
Methylparaben	0.15
Propylparaben	0.05
Part 2: Olive oil	10.0
2. Topical liposomal product with encapsulated consistency enhancer Proliposome gel: Phospholipon 90H	5.0
Cholesterol	2.0
Stearic acid	1.0
Propylene glycol	7.0
Emulsion: Part 1: Distilled water q.s. to	100
PEFA	4.0
Methylparaben	0.05
Propylparaben	0.05
Part 2: Glyceryl stearate	1.0
Cetyl alcohol	0.6
Synthetic beeswax	0.28
3. Topical liposomal product with encapsulated oil droplet and consistency enhancer Proliposome gel: Phospholipon 90H	5.0
Cholesterol	2.0
Stearic acid	1.0
Propylene glycol	7.0
Emulsion: Part 1: Distilled water q.s. to	100
PEFA	4.0
Methylparaben	0.05
Propylparaben	0.05
Part 2: Olive oil	10.0
Glyceryl stearate	1.0
Cetyl alcohol	0.6
Synthetic beeswax	0.28
B. COMPOSITIONS CONTAINING PGE.sub.1	
4. Topical liposomal prostaglandin E.sub.1 Proliposome gel: Phospholipon 90H	15.0
Cholesterol	1.5
Ascorbyl Palmitate	0.05
Monolauroyllysine	1.0
Stearic Acid	0.5
Centrolex P	0.3
Methyl salicylate	2.0
Prostaglandin E.sub.1	0.05
Propylene glycol	7.0
Aqueous Phase q.s. to	100
Sodium chloride	0.9
Triethanolamine	0.05
Glycerol	5.0
Methylparaben	0.1
Propylparaben	0.02
Distilled water	98.48
5. Topical liposomal product with encapsulated lipophilic drug in multicompartments and with encapsulated oil droplet and consistency enhancer Proliposome gel: Phospholipon 90H	5.0
Cholesterol	2.0
Stearic acid	1.0
Propylene glycol	7.0
Prostaglandin E.sub.1	0.05
Propylene glycol	7.0
Emulsion: Part 1: Distilled water q.s. to	100
PEFA	4.0
Methylparaben	0.15
Propylparaben	0.05
Part 2: Olive oil	10.0
Glyceryl stearate	1.0
Cetyl alcohol	0.6
Synthetic beeswax	0.28
Prostaglandin E.sub.1	0.05
6. Topical liposomal product with encapsulated PGE.sub.1 oil and consistency enhancer Proliposome gel: Phospholipon 90H	5.0
Cholesterol	1.5
Monolauroyllysine	1.0
Stearic acid	0.5
Prostaglandin E.sub.1	0.5
Fropylene glycol	7.0
Emulsion: Part 1: Distilled water q.s. to	100
PEFA	4.0
Methylsalicylate	2.0
.alpha.-tocopherylnicotinate	1.0
Methylparaben	0.05
Propylparaben	0.05
Part 2: Macadamia nut oil	3.0
Glyceryl stearate	1.0
Cetyl alcohol	0.6
Synthetic beeswax	0.28
7. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H	15%
Cholesterol	2%
Ascorbyl Palmitate	0.05%
Phospholipon 80	
Prostaglandin E.sub.1	0.05%
Propylene Glycol Aqueous Phase F q.s. to	100
NaCl	0.9%
Ethanol	10%
dd, H.sub.2 O	89.1%
pH	5.5
Encapsulation Efficiency:	16%
8. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H	15%
Cholesterol	1.5%
Ascorbyl Palmitate	0.05%
Propylene glycol	7%
Monolauroyllysine	1%
Glycerol	5%
Stearic Acid	0.5%
Centrolex P	0.3%
Prostaglandin E.sub.1	0.05%
Agueous Phase 16 q.s. to	100
NaCl	0.9%
Methylparaben	0.1%
Propylparaben	0.02%
Triethanolamine	0.05
dd, H.sub.2 O	98.48%
pH	8.3
Encapsulation Efficiency:	81%
9. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H	15%
Cholesterol	1.5%
Ascorbyl Palmitate	0.05%
Propylene glycol Monolauroyllysine Glycerol Lauric Acid	0.5%
Centrolex P	0.3%
Prostaglandin E.sub.1	0.05%
Aqueous Phase 16 (see above) q.s. to	100
Encapsulation Efficiency:	76%
10. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H	15%
Cholesterol	1.5%
Ascorbyl Palmitate	0.05%
Propylene glycol	7%
Monolauroyllysine	1%
Glycerol	5%
Oleic Acid	1%
Centrolex P	0.3%

Prostaglandin E.sub.1 0.05% Aqueous Phase 16 (see above) q.s. to 100 Encapsulation Efficiency: 67% 11. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H 15% Cholesterol 1.5% Ascorbyl Palmitate 0.05% Propylene glycol 7% Monolauroyllysine 1% Glycerol 5% Stearic Acid 0.5% Centrolex P 0.3% Methylsalicylate 2% Prostaglandin E.sub.1 0.05% Aqueous Phase 16 (see above) q.s. to 100 Encapsulation Efficiency: 33% 12. -0.01% Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H 15% Cholesterol 1.5% Ascorbyl Palmitate 0.05% Propylene glycol 7% Monolauroyl lysine 1% Glycerol 5% Stearic Acid 0.5% Centrolex P 0.3% Methylsalicylate 2% Prostaglandin E.sub.1 0.1% Aqueous Phase 16 (see above) q.s. to 100 13. Topical liposomal product with PGE.sub.1 Proliposome Gel: Phospholipon 90H 15% Cholesterol 1.5% Ascorbyl palmitate 0.05% Propylene glycol 7.0% Monolauroyllysine 1.0% Glycerol 5.0% Stearic acid 0.5% Centrolex P 0.3% Prostaglandin E.sub.1 0.05% Calcium thioglycolate 1.0% Aqueous phase 16 (see above) q.s. to 100%

Detailed Description Paragraph Table (6):

% (w/w)

C. COMPOSITION CONTAINING LOCAL ANAESTHETIC

14. Topical liposomal product with encapsulated lipophilic drug in multicompartments and with encapsulated oil droplet and consistency enhancer Prolipsome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Stearic acid 1.0 Tetracaine 1.0 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0.05 Part 2: Olive oil 10.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28 Tetracaine 1.0

D. COMPOSITION CONTAINING AN ANTI-VIRAL AGENT

15. Topical liposomal product with encapsulated antiviral drug combination with or without Consistency enhancer Proliposome gel: Phospholipon 90H 10.0 Phospholipon 90 0.5 Cholesterol 1.0 Stearic acid 1.0 Propylene glycol 7.0 Ara-A 1.0 MMUdR 1.0 Aqueous phase F q.s. to 100 OR: Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0. Part 2: Canola oil 10.0

E. COMPOSITIONS CONTAINING A PROTEIN (INTERFERON ALPHA and INTERFERON GAMMA)

16. Topical liposomal product with encapsulated protein drug and with encapsulated oil droplet and consistency enhancer Proliposome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Monolauroyllysine 2.0 Propylene glycol 7.0 Emulsion: Part 1: Phosphate buffer q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0. Interferon alpha 20 MU Part 2: Olive oil 10.0 GIyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28 17. Topical liposomal product with encapsulated protein drug and consistency enhancer Proliposome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Monolauroyllysine 2.0 Propylene glycol 7.0 Emulsion: Part 1: Phosphate buffer q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0.05 Interferon gamma 2 MU Part 2: Glyceryl stearate 1.0 Cetyl alcohol 0.6

F. COMPOSITIONS CONTAINING HERBAL EXTRACTS

18. Topical liposomal product with encapsulated oily plant extract and consistency enhancer Proliposome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Stearic acid 1.0 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0. Part 2: German chamomile oily extract 5.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28 19. Topical liposomal product with encapsulated oil and oil-soluble cosmetic active ingredient and consistency enhancer Proliposome gel: Phospholipon 90H 5.0 Cholesterol 2.0 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0.05 Part 2: Azulenol 0.1 Rose hip seed oil 5.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28 20. Topical liposomal product with encapsulated oil and oil-soluble cosmetic active ingredient and consistency enhancer Proliposome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0.05 Part 2: Alpha bisabolol 10.0 Rocou ami oil 3.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28

G. COMPOSITIONS CONTAINING VITAMINS

21. Topical liposomal product with encapsulated oil- soluble cosmetic active ingredient and consistency enhancer Proliposome Gel: Phospholipon 90H 5.0 Cholesterol 2.0 Stearic acid 1.0 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.05 Propylparaben 0.05 Part 2: Vitamin E 10.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28 22. Topical liposomal product with encapsulated oil- soluble cosmetic active ingredients (vitamins) and consistency enhancer Proliposome Gel:

Phospholipon 90H 5.0 Cholesterol 2.0 Stearic acid 1.0 Ascorbyl palmitate 0.5 Propylene glycol 7.0 Emulsion: Part 1: Distilled water q.s. to 100 PEFA 4.0 Methylparaben 0.15 Propylparaben 0.05 Part 2: Vitamin E 10.0 Vitamin A 2.0 Glyceryl stearate 1.0 Cetyl alcohol 0.6 Synthetic beeswax 0.28

Detailed Description Paragraph Table (14):

TABLE 10

Formulation of topical liposomal IFN products. PRODUCT METHOD OF ENCAPSULATION NO. Lipid phase mg/g product Aqueous phase .mu.l/g product MANUFACTURE EFFICIENCY*

1

Phospholipon 90H 70 10.48 IFN stock Fusion 55.9 .+-. 1.5% Cholesterol 18 Stearic acid 18 (20 .times. 10.sup.6 IU) Propylene glycol 70 H.sub.2 O q.s. 2 Phospholipon 90H 70 10.48 IFN stock Solvent 57.8% Cholesterol 18 evaporation Stearic acid 18 (20 .times. 10.sup.6 IU) Propylene glycol 70 H.sub.2 O q.s. 3 Phospholipon 90H 100 10.48 IFN stock Fusion 57.3% Cholesterol 18 Oleic acid 6 (20 .times. 10.sup.6 IU) Stearic acid 6 H.sub.2 O q.s. Erucic acid 6 Ascorbyl palmitate 0.5 Propylene glycol 70 4 Phospholipon 90 200 5.24 IFN stock Fusion Ascorbyl palmitate 1 H.sub.2 O q.s. 5 Phospholipon 90H 100 10.48 IFN stock Fusion 59.2% Cholesterol 20 Stearic acid 10 (20 .times. 10.sup.6 IU) Bovine brain extract 5 H.sub.2 O q.s. Type VIII Propylene glycol 70 6 Phospholipon 90H 50 10.48 IFN stock Fusion 69.8 .+-. 2.3% Phospholipon 90 50 Cholesterol 20 (20 .times. 10.sup.6 IU) Bovine brain extract 10 H.sub.2 O q.s. Type III Propylene glycol 70 7 Phospholipon 90H 50 10.48 IFN stock Fusion 65.9% Phospholipon 90 50 Cholesterol 20 (20 .times. 10.sup.6 IU) Stearylamine 10 PBS q.s. Propylene glycol 70 8 Phospholipon 90H 50 10.48 IFN stock Fusion 79.0% Phospholipon 90 50 COMPOUND A 20 (20 .times. 10.sup.6 IU) Cholesterol 20 PBS q.s. Propylene glycol 70 9 Phospholipon 90H 50 10.48 IFN stock Fusion 77.8 .+-. 1.3% Phospholipon 90 50 COMPOUND A 10 (20 .times. 10.sup.6 IU) Cholesterol 20 PBS q.s. Propylene glycol 70 10 Phospholipon 90H 100 10.48 IFN stock Fusion 47.0 .+-. 1.3% COMPOUND B 20 Cholesterol 20 (20 .times. 10.sup.6 IU) Propylene glycol 70 PBS q.s. 11 Phospholipon 90H 100 10.48 IFN stock Fusion 75.2% COMPOUND A 10 COMPOUND B 10 (20 .times. 10.sup.6 IU) Cholesterol 20 PBS q.s. Propylene glycol 70 12 Phospholipon 90H 50 10.48 IFN stock Fusion 45.7% Phospholipon 90 50 COMPOUND B 10 (20 .times. 10.sup.6 IU) Cholesterol 20 PBS q.s. Propylene glycol 70 13 Phospholipon 90 100 10.48 IFN stock Fusion 73.1% COMPOUND A 20 Cholesterol 20 (20 .times. 10.sup.6 IU) Propylene glycol 70 PBS q.s. 14 Phospholipon 90H 100 10.48 IFN stock Fusion 54.8% Centrolex P 10 Cholesterol 20 (20 .times. 10.sup.6 IU) Propylene glycol 70 PBS q.s.

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*encapsulation efficiency measurements are the average of 2-5 separate experiments COMPOUND A = dipalmitoyllysine COMPOUND B = monolauroyllysine Properties of the formulations described in Table 10 are given in Table 11.

WEST Search History

DATE: Tuesday, April 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L2	L1 and ((424/$)!.CCLS.)	151	L2
L1	ascorbic adj5 (ascorbyl adj5 palmitate)	472	L1

END OF SEARCH HISTORY

Current US Original Classification (1):
424/59

CLAIMS:

4. A method according to claim 1 wherein the fatty acid ester of ascorbic acid is ascorbyl palmitate.

12. A method according to claim 7 wherein the ascorbic fatty acid ester is ascorbyl palmitate.

15. A method of preparing a composition containing from about 20% to about 50% of a fatty acid ester of ascorbic acid selected from the group consisting of ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, ascorbyl behenate, and mixtures thereof, and at least one water-soluble ingredient comprising dissolving, homogenously mixing or stably dispersing the fatty acid ester in a solvent selected from the group consisting of polyethylene glycol, ethoxydiglycol, butylene glycol, propylene carbonate, a capric glyceride, a caprylic glyceride, an isosorbide, an alkyl lactate, and mixtures thereof, and then homogenizing the dissolved ester with an aqueous phase containing the water-soluble ingredient such that the composition is stabilized from precipitation or color change when stored at room temperature for at least about three months.

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L2: Entry 64 of 151 File: USPT Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180133 B1
TITLE: Antioxidant composition for topical/transdermal prevention and treatment of wrinkles

Brief Summary Text (25):
Vitamin C is present as an ester of L-Ascorbic acid. L-Ascorbic Acid 6-Palmitate (ascorbyl palmitate) is particularly preferred. Ascorbyl palmitate differs from ascorbic acid and its salts in various ways. Ascorbyl palmitate is a synthethic ester which is fat soluble in contrast to ascorbic acid and its salts which are water soluble. This ester forms ascorbyl palmitate which is stable, compatible with other skin treating agents and has a neutral pH as opposed to ascorbic acid which has a very low pH. Due to its fat solubility, ascorbyl palmitate penetrates the skin more readily than ascorbic acid and its salts reaching comparativelly high levels in much shorter periods of time.

Current US Original Classification (1):
424/448

Current US Cross Reference Classification (1):
424/443

Current US Cross Reference Classification (2):
424/444

Current US Cross Reference Classification (3):
424/445

Current US Cross Reference Classification (4):
424/447

Current US Cross Reference Classification (5):
424/449

Current US Cross Reference Classification (6):
424/78.02

L2: Entry 114 of 151 File: USPT Nov 12, 1996

DOCUMENT-IDENTIFIER: US 5574063 A
TITLE: Method and compositions for topical application of ascorbic acid fatty acid esters for treatment and/or prevention of skin damage

Current US Cross Reference Classification (1):
424/59

Current US Cross Reference Classification (2):
424/60

CLAIMS:

16. A method for the treatment of damaged or aging skin and epithelial tissue disorders which are directly or indirectly caused or mediated by collagen deficiency, oxygen-containing free radicals, oxidative generation of biologically active metabolites, or mixtures of these, said treatment comprising topically applying to the affected tissue areas, the combination of

A. an effective amount of a fat-soluble fatty acid ester of ascorbic acid selected from the group consisting of ascorbyl palmitate, ascorbyl laurate, ascorbyl myristate, ascorbyl stearate, and mixtures thereof, and

B. a compound selected from the group consisting of .alpha.-, .beta.-, .gamma.-, and .delta.-tocotrienols, desmethyl-tocotrienol, didesmethyl-tocotrienol, their derivatives having methylated or demethylated chroman rings, acylated derivatives and .alpha.-hydroxy acids, and mixtures thereof,

all in a carrier composition that solubilizes and dispenses the above active ingredients.

19. A method according to claim 16 wherein the ascorbic acid ester is ascorbyl palmitate.

21. A method according to claim 20 wherein said fat soluble fatty acid ester of ascorbic acid is selected from the group consisting of ascorbyl palmitate, ascorbyl laurate, ascorbyl myristate, ascorbyl stearate, and mixtures thereof.

L2: Entry 45 of 151 File: USPT Oct 2, 2001

DOCUMENT-IDENTIFIER: US 6296861 B1
TITLE: Treatment of skin damage using conjugated linoleic acid and ascorbyl fatty acid esters

Abstract Text (1):
A synergistic combination of conjugated linoleic acid and fatty acid esters of ascorbic acid is topically applied to treat skin damage, such as contact dermatitis, atopic dermatitis, xerosis, eczema, rosacea, seborrhea, psoriasis, thermal and radiation burns, other types of skin inflammation, and aging. Typical compositions contain from about 1% to about 25% by weight of a CLA preparation containing 9,11-octadecadienoic acid and 10,12-octadecadienoic acid, and from about 0.5% to about 15% by weight of a saturated fatty acid ester of ascorbic acid such as ascorbyl palmitate.

Detailed Description Text (6):
Fatty acid esters of ascorbic acid include ascorbic acid acylated with single or multiple fatty acid groups, wherein the fatty acids typically have 8 to 24 carbon atoms, and their salts. The more oxidation-resistant saturated fatty acid esters of ascorbic acid are preferred, including, but not limited to, ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, and ascorbyl behenate, and their salts, e.g., magnesium ascorbyl stearate. Ascorbyl palmitate is used in one preferred embodiment. As denoted herein, where fatty acid esters are described, e.g., ascorbyl stearate, compositions having predominantly that ester, e.g., predominantly stearate, are included. The esters may be prepared using hydrogenated oils or fats, or fractions thereof, and contain small amounts of another ester. Ascorbyl stearate prepared using canola, for example, commonly contain about 4% ascorbyl palmitate.

Current US Original Classification (1):
424/401

CLAIMS:

4. A method according to claim 3 wherein the fatty acid ester of ascorbic acid is selected from the group consisting of ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, ascorbyl behenate, and mixtures thereof.

5. A method according to claim 4 wherein the fatty acid ester of ascorbic acid is ascorbyl palmitate.

L2: Entry 65 of 151 File: USPT Dec 19, 2000

DOCUMENT-IDENTIFIER: US 6162419 A
TITLE: Stabilized ascorbyl compositions

Brief Summary Text (4):
Fatty acid esters of ascorbic acid such as ascorbyl palmitate are employed in topical compositions for a varieity of purposes such as for treating and/or preventing sunburn (U.S. Pat. No. 5,409,693 to Perricone; this and all other references cited hereafter are hereby expressly incorporated herein by reference in their entireties) and for treating disorders of the skin which are caused by, or are dependent upon, depleted or inadequate collagen levels, and/or oxygen-containing free radicals, and/or oxidative generation of active metabolites via lipoxygenase pathways (U.S. Ser. No. 08/407,413 to Perricone filed Mar. 17, 1995 and allowed Jun. 11, 1996 now U.S. Pat. No. 5,574,063). Topical compositions containing acetylcholine precursors such as dimethylaminoethanol have also been disclosed for the treatment of aging skin and subcutaneous muscles; in some embodiments, the compositions also contain fatty acid esters of ascorbic acid (U.S. Pat. No. 5,554,647 to Perricone).

Brief Summary Text (18):
By use of the solvent systems, compositions containing up to about 25% by weight of a saturated fatty acid ester of ascorbic acid such as ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, ascorbyl behenate, the corresponding ascorbyl salts such as magesium ascorbyl palmitate or stearate, and mixtures thereof, can be stably prepared in formulations containing water-soluble ingredients such as ascorbic acid and/or ascorbic acid salts, e.g., magnesium ascorbate, calcium ascorbate, sodium ascorbate, and/or potassium ascorbate. Ascorbyl palmitate is used in preferred embodiments.

Detailed Description Text (3):
This invention encompasses methods of solubilizing up to at least about 25% of a fatty acid ester of ascorbic acid and compositions containing the esters thereof. Fatty acid esters of ascorbic acid include ascorbic acid acylated with single or multiple fatty acid groups, wherein the fatty acids typically have 8 to 24 carbon atoms, and their salts. The more oxidation-resistant saturated fatty acid esters of ascorbic acid are preferred, including, but not limited to, ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, and ascorbyl behenate, and their salts, e.g., magnesium ascorbyl stearate. Ascorbyl palmitate is used in one embodiment. As denoted herein, where fatty acid esters are described, e.g., ascorbyl stearate, compositions having predominantly that ester, e.g., predominantly stearate, are included. The esters may be prepared using hydrogenated oils or fats, or fractions thereof, and contain small amounts of another ester. Ascorbyl stearate prepared using canola, for example, commonly contain about 4% ascorbyl palmitate.

Detailed Description Text (15):
A typical composition of the invention contains from about 1% to about 25% by weight of a saturated fatty acid ester of ascorbic acid such as ascorbyl laurate, ascorbyl myristate, ascorbyl palmitate, ascorbyl stearate, ascorbyl behenate, and/or mixtures; a solvent selected from the group consisting of polyethylene glycol, ethoxydiglycol, propylene glycol, butylene glycol, propylene carbonate, glycerin, a capric glyceride, a caprylic glyceride, an alkyl lactate, an alkyl adipate, an isosorbide, and mixtures thereof; from about 0.1% to about 5% by weight dimethylaminoethanol; L-tyrosine; a penetration enhancer such as oleic acid and/or urea; and an antioxidant.